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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/155,076	10/23/98	GREENFIELD S	263/PPIR2548

HM11/0622

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EXAMINER	
TURNER,S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/22/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/155,076	Greenfield et al
Examiner	**Art Unit**
Sharon L. Turner, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on 3-30-01

2a) [X] This action is **FINAL.** 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) 13, 16, and 30-38 is/are pending in the applica

4a) Of the above, claim(s) 34-38 is/are withdrawn from considera

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) 13, 16, and 30-33 is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [X] Claims 13, 16, and 30-38 are subject to restriction and/or election requirem

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [ ] Notice of References Cited (PTO-892)

16) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) [ ] Interview Summary (PTO-413) Paper No(s). _____

19) [ ] Notice of Informal Patent Application (PTO-152)

20) [ ] Other:

Response to Amendment

1. The amendments filed 2-5-01 and 3-30-01 have been entered into the record and have been fully considered.

2. Claims 14, 15 and 17-29 are canceled. Claims 13, 16 and 30-38 are pending.

3. Newly submitted claim 33 is the first method of using the first special technical feature peptide and thus will be examined with group I.

4. Newly submitted claims 34-38 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons:

The application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group VI, claim 34-35 drawn to the second method of screening using the first technical feature peptides and method of identifying a compound using the second method of screening.

Group VII, claim 36 drawn to a method of preparing the fifth technical feature composition.

Group VIII, claim 37, drawn to a method of inhibiting calcium channel modulation using the sixth technical feature of an identified compound.

Group IX, claim 38, drawn to a method of inhibiting calcium channel modulation using the seventh technical feature composition.

5. The inventions listed as Groups VI-IX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special

technical features for the following reasons: The technical features comprise variable compounds. Although the compounds may be similarly screened or identified their primary structure varies. Thus the compounds, compositions and variable methods of making, using and screening are separable as they lack a common core structure technical feature.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 34-38 are withdrawn from consideration as being directed to non-elected inventions. See 37 CFR 1.142(b) and MPEP § 821.03.

6. As a result of applicants amendment, all rejections not reiterated herein have been withdrawn by the examiner.

Rejections Withdrawn

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

8. Claims 13, 16 and 30-31 were rejected under 35 U.S.C. 101 because the claimed invention was not supported by either a specific and substantial asserted utility or a well established utility.

Applicants argue that the 14-mer functions as a calcium channel modulator, that calcium influx may be beneficial to developing neurons and that one of skill in the art would recognize

the utility of the peptides as a research tool to identify compounds of interest to the development of therapeutics for neurodegenerative diseases associated with non-enzymatic functions of AchE.

Applicants arguments filed 2-5-01 have been fully considered but are not persuasive. However, in view of 5,932,780 which teaches the utility of E6 processed fragments in screening for anticholinesterase substances, the rejection has been withdrawn.

Rejections Maintained

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 13, 16, 30-31 and 33 stand rejected under 35 U.S.C. 112, first paragraph, as set forthin Paper No. 12, mailed 10-4-00 and as reiterated herein because the specification, while being enabling for calcium influx mediated via the 14-mer peptide, does not reasonably provide enablement for the prediction of such activities from structural variants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification fails to teach the skilled artisan those structural determinants which provide the functional activity of calcium ion influx, in particular as it relates to the recitation of peptides which are at least 6 amino acids and which are 70% homologous to SEQ ID NO:1. The structural limitations define a genus for which only a single molecule is observed to retain

functional activity The art recognizes the unpredictability of function as it relates to amino acid structure i.e., peptide function is critically dependent and determined by peptide structure, see in particular Skolnick et al., Trends in Biotech, 18(1):34-39, 2000, abstract, Box 2. Thus, partial peptides sequences and sequences bearing percent homology would not be expected to function the same as similar peptides. The specification provides no guidance by which the artisan can more likely than not predict those structures which fall within the scope of the claim and there is no evidence of other members of the genus which retain calcium influx activity. Thus, the skilled artisan cannot make and use the claimed peptides without further undue experimentation to identify each peptides functional activity and relevant use.

Claim Rejections - 35 USC § 102 or 103

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 13 and 16 stand rejected under 35 U.S.C. 102(b) as set forth in Paper No. 12, mailed 10-4-00 as being anticipated by de Serres et al., Cellular and Molecular Neurobiology, 13(3):279-87, June 1993.

Applicants argue that the peptides of de Serres do not meet the limitations of applicants claims as the peptides comprise various longer portions which do not overlap and that none of the peptides exhibit the calcium modulatory activity specified. Further applicants argue that the

whole acetylcholinesterase can not be considered the invention as the whole AchE does not share calcium channel modulator activity and would not be considered a peptide.

Applicants arguments filed 2-5-01 have been fully considered but are not persuasive. It is noted that applicants claims with the exception of new claim 32 are peptides which "comprise" peptides of SEQ ID NO:1 and functional variants with at least 70% homology with 6 amino acids of SEQ ID NO:1. Thus the structural requirements comprise other sequences and the full length peptide would fall within the scope of the claims. Further it is noted that applicants arguments appear contradictory to that disclosed in the specification in particular at p. 11, lines 20-25 which teach that the peptide fragment derived from AchE has a selective and reversible action reminiscent of the actions of AchE itself, i.e., with lower doses/less sensitive situations there is an enhanced calcium influx, and therefore it appears that full length AChE would by applicants admission provide for the recited calcium channel modulatory activity. The skilled artisan contrarily would recognize the AChE molecule as a peptide as the structure is that of a polypeptide amino acid sequence.

13. Claims 13 and 16 stand rejected under 35 U.S.C. 102(b) as set forth in Paper No. 12, mailed 10-4-00 as being anticipated by Moran et al., Acta Neuropathol., 85:362-369, 1993.

Applicants argue that Moran does not teach any fragment of AchE as that claimed.

Applicants arguments filed 2-5-01 have been fully considered but are not persuasive. The claims are not limited to AchE fragments but instead recite isolated peptides comprising such sequences which claims read on the full length molecule.

New Rejections Based on Amendment

14. Claims 13, 16, 30, 31 and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims have been amended to recite "the peptide of SEQ ID NO:1 and functional variants thereof, said functional variants comprising...", and "retaining the calcium channel modulatory function of the peptide," which recitation appears to be new matter as the specification does not appear to support the breadth of the claimed peptides with respect to the functional limitations of the claims. Applicants point to support for such amendment in the Title and specification at p. 6, lines 24-25 and Example 3. However, the title and specification do not reflect the functional embodiment of calcium channel modulatory function for peptides other than SEQ ID NO:1, i.e., for the breadth of that encompassed by the claims including functional variants thereof wherein said variants comprise at least 6 amino acid residues having at least 70% homology with part or all of the peptide of SEQ ID NO:1. In contrast the specification only appears to support a compound which inhibits such activity as disclosed at p. 6, lines 24-25 and the activity of the 14-mer peptide of SEQ ID NO:1 and full length AchE in providing calcium channel modulatory activity, specifically enhanced calcium influx..

15. Claims 13, 16 and 30-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13, 16 and 30-32 recite the limitation "the calcium channel modulatory function" in reference to claim 13. There is insufficient antecedent basis for this limitation in the claims.

In addition, the recitation of "the calcium channel modulatory function" is indefinite to the skilled artisan as the metes and bounds of the functional recitation in the claims cannot be discerned. The artisan recognizes a multitude of properties and functions associated with calcium, calcium ions and calcium ion channels, see for example index p. 1071-1072 of Kandel et al., Ed., Principles in Neural Science, Elsevier, 1991. Yet none of these functions is clearly established as "the calcium channel modulatory function" required of the claimed peptides. Thus, the skilled artisan cannot determine those peptides which are functionally included or excluded from the claims.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

17. Claims 13, 16, 30-31 and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Soreq et al., US Patent No. 5,932,780, filed Jan. 9, 1995 and issued August 3, 1999.

Applicants arguments have clarified that the intended invention is not full length AChE as encompassed by the claims, but shorter fragments of AchE. The following rejection is thereby necessitated by applicants arguments even though the claims remain drawn to peptides comprising which peptides include full length AchE.

Soreq et al., teach SEQ ID Nos:7, 8 and 25 which correspond to isolated C-terminal (Exon 6) peptides of AchE. The peptides are partial fragments of acetylcholinesterase and consist of 40-45 amino acids in length. The peptides comprise SEQ ID NO:1 in full, see in particular residues 12-25 of SEQ ID NO:25, residues 17-30 of SEQ ID NO:7 and residues 17-30 of SEQ ID NO:8 and Figure 6. Column 8, lines 9-20 teaches biologically active analogs of such sequences. The Soreq reference is silent with respect to the calcium channel modulatory function of the peptides, however it is noted that as the structural limitations of the peptides are met by Soreq et al., the functional limitations are deemed inherent absent convincing factual evidence to the contrary. It is further noted as set forth above in column 8, lines 9-20 that since the biological (enzymatic) activity of the Soreq peptides is retained and the biological activity of the full length enzymatic AchE molecule includes mediation of calcium influx, as disclosed in applicants specification at p. 11, lines 20-25, that it is presumed that the Soreq peptides also retain mediation of calcium influx to cells.

18. Claim 33 is rejected under 35 U.S.C. 102(b) as being anticipated by Dagerlind et al., Neuroscience, 62(1):217-239, 1994.

Dagerland et al., teach 5 monoclonal antibodies to acetylcholinesterase generated using various acetylcholinesterase peptides, see in particular p. 218, column 1. The peptides are encompassed by the claims as the peptides may be any size in length and comprise full length. Thus the reference teachings teach the process limitations of a method for obtaining an antibody using peptide antigens of applicants claims.

Status of Claims

Allowable Subject Matter

19. Claim 32 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. In the claim "having" is interpreted as consisting.

Conclusion

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

21. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
June 18, 2001

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud